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Award Number: DAMD17-01-1-0627

TITLE: Is Breast Tissue from Women Who Carry Germ-Line BRCA1 or  
BRCA2 Mutations "Normal"? - An Immuno-Histopathological Study

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REPORT DATE: August 2003

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command  
Fort Detrick, Maryland 21702-5012

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20040213 044

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 074-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503				
1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE August 2003		3. REPORT TYPE AND DATES COVERED Annual (1 Aug 02-31 Jul 03)
4. TITLE AND SUBTITLE Is Breast Tissue from Women Who Carry Germ-Line BRCA1 or BRCA2 Mutations "Normal"? - An Immuno-Histopathological Study			5. FUNDING NUMBERS DAMD17-01-1-0627	
6. AUTHOR(S) William D. Foulkes, Ph.D. Lesley Alpert Louise Quenneville Gilles Tremblay				
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9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited				12b. DISTRIBUTION CODE
13. ABSTRACT (Maximum 200 Words)  After review of 140 files, a total of 90 prevalent cases of breast cancer were recruited from both clinical genetic services at the Montreal Hospital sites. A total of 36 cases were examined by three separate blinded pathologists for certain morphological and histological features to be compared among carriers and non-carriers of the BRCA1/2 genes. The pre-cancerous features that we focused on included apocrine hyperplasia, sclerosing adenosis, columnar alteration with prominent apical snouts and secretions (CAPSS) and usual ductal hyperplasia. We are now in the process of having the remaining 24 cases examined and reviewing the raw data to establish some results and conclusions. We hope to complete the examination of the remaining cases and the analysis of the raw data very shortly. Immunohistochemical analysis will follow.				
14. SUBJECT TERMS No subject terms provided.			15. NUMBER OF PAGES 5	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

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## **Is breast tissue from women who carry germ-line *BRCA1* or *BRCA2* mutations “normal”?-An immuno-histopathological study.**

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Investigator award number: DAMD17-01-1-0627

### **Introduction**

In this study we were funded to perform an extensive morphological and immunohistochemical study of non-neoplastic breast tissue from the primary invasive cancer among women whose *BRCA1/2* status had already been established. We were also funded to compare morphological and biological features of breast tissue in *BRCA1* or *BRCA2* mutation carriers to age matched controls.

### ***Task 1: Case ascertainment, contact, consent, acquiring pathology material, and review of tissue by pathologists, years 1-2.***

- Obtained approval for this study at relevant IRB to start the project at the SMBD-Jewish General Hospital.
- All the prevalent cases were ascertained using records from the clinical genetic service at the SMBD-Jewish General Hospital. A total of 117 cases were ascertained.
- An introduction letter with a reply card was sent to the 117 prevalent cases that we wished to recruit from the SMBD-Jewish General Hospital. Once reply cards were received, a research assistant contacted the cases to obtain signed consent. A total of 61 women gave their signed consent. 15 women refused to participate in this study. 41 women did not reply at all to the letter and we were unable to contact them due to change of address, telephone number or messages were not returned.
- We submitted the study for ethical approval to recruit more cases at the Montreal General Hospital. This meant making some changes to the consent forms and this process took a little over three months to complete.
- A total of 29 cases were ascertained from the clinical genetic service at the Montreal General Hospital. Twenty-nine prevalent cases were contacted and a total of 29 women were recruited from the Montreal General Hospital site.

- Once consent was received the pathology material (breast tissue) for that case was ordered so that the morphological and immuno-histochemical examination could commence.
- Due to a limited availability of time by the pathologists co-investigating on this study, we submitted a no-cost extension and that was accepted in August, 2002 so that the study would not expire before important results could be obtained.
- A total of 36 cases were examined. 3 cases could not be reviewed completely due to missing blocks or slides. The pre-cancerous pathological features that we focused on included apocrine hyperplasia, sclerosing adenosis, columnar alteration with prominent apical snouts and secretions (CAPSS) and usual ductal hyperplasia.
- We are now in the process of having the remaining 24 cases examined and reviewing the raw data to establish some results and conclusions. We hope to complete the examination of the remaining cases and the analysis of the raw data very shortly. Immunohistochemical analysis will follow.

#### **Key research accomplishments**

- A total 90 cases were recruited from both clinical genetic services at the Montreal Hospital sites.
- 36 cases were examined by three separate blinded pathologists for key morphological and histological features.
- Data analysis is underway.

#### **Reportable outcomes**

##### **1. Published work**

Nil

##### **2. Conclusions**

At the present time we are commencing the analysis of the raw data obtained by the pathologists. The pathologists expect to be finished analyzing the remaining 24 cases in a short time. We will then combine the two data sets together for final statistical analysis. Immunohistochemical analyses will follow as soon as these initial analyses are complete.